175

Dinis P[1], Ribeiro M[1], Avelino A[2], Reis M[1], Cruz F[1]
1. Department of Urology, Hospital S. João, 2. Institute of Histology and Embryology

EFFECT OF INTRAVESICAL RESINIFERATOXIN ON LUTS OF PATIENTS WITH BPH. PRELIMINARY REPORT

Aims of Study

Bladder overactivity in patients with chronic bladder outlet obstruction due to BPH is a main cause of LUTS but is still poorly understood. Present therapeutic options, that include alpha-1 blockers and anticholinergics, are unsatisfactory in a large proportion of these patients. On the other hand, recent experimental [1] and clinical [2] data have suggested that a spinal micturition reflex triggered by type C afferent fibers may be overactive in BPH patients. Nerve growth factor (NGF) occurring in high concentrations in hypertrophied bladders may have a pivotal role in the process, by sensitizing C-fibers [3,4]. These data suggest, therefore, that desensitization of bladder C-fibers with intravesical vanilloids may constitute another alternative to control bladder overactivity and LUTS in BPH patients. As a matter of fact, vanilloids not only suppress C-fiber activity but also decrease NGF up-take by sensory fibers, therefore counteracting the sensitizing effect of the neurotrophin [5]. In the present work an open label study was undertaken to evaluate the effect of intravesical resiniferatoxin (RTX) on LUTS secondary to BPH.

Methods

Eleven patients with LUTS associated with BPH gave written informed consent to this study. None of them had any form of neurological disease or had initiated anticholinergic or alpha-blocker medication in the past ten days. All patients were screened by haematological and biochemical blood tests, microbiological urinary investigation and ultrasonographic evaluation of the urinary system. A uroflowmetry, IPSS and QoL scores, post void residual urine and a voiding chart of seven consecutive days were obtained. All patients had a normal upper urinary tract, a maximum flow rate (Qmax.) greater than 8 ml/s, sterile urine, post void residual urine lesser than 150 ml and normal renal function. Four of them had urge incontinence (2 to 11 episodes per week). Treatment consisted of a single instillation of 100 ml of a 50 nM RTX solution in 10% alcohol in saline, left inside the bladder during 30 minutes. All patients were followed at 1 month after treatment and 9 were reviewed at 3 months.

Results

Treatment did not cause pain or any significant discomfort. Mean IPSS score decreased from 19±4.9 to 9.7±3.4 ($p<0.0001$) at 1 month and to 10.1±2.2 ($p<0.001$) at 3 months. Mean urinary frequency decreased from 13.1±4.4 to 8.8±2.3 ($p< 0.01$) and to 8.7±2 ($p<0.01$) at the same time points. Urinary incontinence disappeared in 3 patients and decreased from 9 to 4 episodes per week in the fourth patient. Mean QoL score decreased from 4.5±1 to 2.4±0.9 ($p<0.0001$) at 1 month and to 2.3±1.1 ($p<0.0001$) at 3 months. Mean Qmax, which was 13.1±3.2 ml/s at baseline, did not change with the treatment. At 1 and 3 months post void residual urine remained inferior to 100 ml in all patients.

Conclusions

This preliminary study suggests that intravesical desensitisation with RTX might be useful in the treatment of LUTS in patients with BPH and warrants the launching of a large placebo-controlled study. In addition it confirms the role of a C-fiber mediated micturition reflex to the emergency of LUTS in BPH patients.

References

1- Steers WD, and de Groat WC.J Urol 140:864–871, 1988.
2- Chai TC, Gray ML, and Steers WD. J Urol 160:34–38, 1998.
3 Steers WD, Kolbeck S, Creedon D, *et al*: J Clin Invest 88:1709–1715, 1991.
4-Tanner R, Chambers P, Khadra MH, *et al.*. BJU Int., 85:1115-1119; 2000.
5- Cruz, F. Urology, 59 (Suppl 5A): 51-60; 2002.